



CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Meningoencephalitis as a complication of acute otitis media in an 11-year-old child

Zoran Dudvarski^{1,2}, Nenad Arsović^{1,2}, Snežana Ješić^{1,2}, Vladimir Nešić^{1,2}, Biljana Međo^{1,3},
Dimitrije Nikolić^{1,4}

¹University of Belgrade, Faculty of Medicine, Belgrade, Serbia;

²Clinical Center of Serbia, Clinic of Otorhinolaryngology and Maxillofacial Surgery, Belgrade, Serbia;

³University Children's Hospital, Intensive Care Unit, Belgrade, Serbia;

⁴University Children's Hospital, Department of Neurology, Belgrade, Serbia

SUMMARY

Introduction Acute otitis media is a very common disease in the early childhood age, with typical symptoms such as otalgia and fever. Otogenic complications are divided into extracranial and intracranial. Although the introduction of antibiotics has significantly reduced the incidence of intracranial complications, they are still present. Clinical picture usually develops fast, with the predominance of neurologic symptoms.

Case outline An 11-year-old boy was admitted to a tertiary health care children's hospital because of fever, agitation, altered behavior and disorder of consciousness. Based on the anamnesis, clinical examination, CT, MRI, and lumbar puncture, it has been established that it is a case of meningoencephalitis as complications of acute otitis media. Besides intense antibiotic and symptomatic therapy, surgical treatment too was conducted as well. Firstly, mastoidectomy with the implantation of ventilation tube was done, followed by radical tympanomastoidectomy, because there was no improvement. The treatment was followed by numerous complications, such as toxic hepatitis, mycoplasma pneumoniae infection, and hemolytic anemia. The treatment lasted for 71 days, and the patient was discharged from the hospital in a good general condition, without the focal motor failure.

Conclusion Meningoencephalitis is unusual and rare complication of acute otitis media that requires urgent diagnostic procedure and multidisciplinary approach to the treatment. Surgical treatment of the ear that caused complications should not be postponed, and the choice of surgical method must be adapted to each patient individually. Hospital treatment of these patients is often prolonged and auditory and neurological sequelae are substantial and require long-term treatment.

Keywords: acute otitis media; intracranial complications; children

INTRODUCTION

Acute otitis media (AOM) is characterized by a sudden onset of symptoms and signs of the middle ear inflammation. This disease is very common in early childhood, and typical symptoms include otalgia and fever. Otoscopic finding of hyperemic, bulging or perforated tympanic membrane with secretion, indicate AOM. When AOM diagnosis is uncertain, it is necessary to perform pneumatic otoscopy or tympanometry in order to assess the presence of secretion in the middle ear. The application of the adequate guides greatly helps the diagnostics and treatment of AOM, and represents the integral part of a routine clinical practice [1, 2]. The occurrence of complications in AOM depends on several factors, such as age, virulence of pathogens, immunological system of the patient, presence of comorbidities and previous therapy. Otogenic complications are the most common in recurrent acute bacterial otitis and exacerbation of chronic inflammatory processes of the middle ear. Sometimes they can be the first sign of inflammation of the middle ear. The most common extracranial

complications (ECC) of AOM are mastoiditis and subperiosteal abscess, while the most common intracranial complications (ICC) of AOM are meningitis, cerebral abscess, epidural abscess and sigmoid sinus thrombosis [3, 4].

Despite the introduction of an effective antibiotic therapy, the rate of otogenic ICC is still about 8%, and the mortality rate is 5–26% [5, 6]. Symptoms and signs that indicate the development of otogenic ICC are dizziness, instability of walk, headache, vomiting, fever, visual field disorders, altered behavior, and disorder of consciousness. In cases of AOM with ICC, clinical picture usually develops quickly, with a predominance of neurological symptoms. High degree of clinical suspicion of ICC, computed tomography (CT) with intravenous contrast, magnetic resonance imaging (MRI) with venography and lumbar puncture with the analysis of cerebrospinal fluid enable an early diagnosis. Therapeutic approach in these cases has to be multidisciplinary and adapted to each patient individually, and besides intense antibiotic and symptomatic therapy, surgical treatment is required as well. In spite of all measures taken in treatment, the prognosis is sometimes uncertain.

Received • Примљено:
May 23, 2017

Accepted • Прихваћено:
August 18, 2017

Online first: August 25, 2017

Correspondence to:

Zoran DUDVARSKI
Clinic of Otorhinolaryngology
and Maxillofacial Surgery
Clinical Center of Serbia
2 Pasterova Street
11000 Belgrade, Serbia
zdudvarski@open.telekom.rs

The objective of this paper is to show fulminant course of AOM with the development of meningoencephalitis in an 11-year-old boy, dilemmas, and complications that existed during treatment, as well as significant auditory and neurological sequelae.

CASE REPORT

In December 2014, an 11-year-old boy was admitted to a tertiary-care children's hospital, because of fever, agitation, altered behavior, and disorder of consciousness. The score on the Glasgow Coma Scale was 5/15. The previous day, the patient complained of headache and pain in the left ear, and then he vomited. During the night, the boy woke up confused, agitated, and vomited again. Other than that, patient's personal and family history had no particularities, no data on previous ear disease, and he was regularly vaccinated according to the calendar of vaccination. The blood test on admission showed: total leukocytes $12.3 \times 10^9/L$ (94.5% neutrophils); C-reactive protein 249 mg/L; procalcitonin 51.2 ng/mL. CT scan showed moderate diffuse cerebral edema and signs of inflammation in the left middle ear, mastoid and petrosal apex, without tegmen erosion (Figure 1). After that, lumbar puncture was performed: cerebrospinal fluid was turbid with a mass of leukocytes (94% polymorphonuclear). The treatment started with vancomycin, meropenem, and metronidazole, according to recommendations from the literature [7].

In the cerebrospinal and blood samples, the cause of infection was not detected. On the second hospital day, there was a spontaneous perforation of the tympanic membrane and purulent secretion from the left ear. *Streptococcus pneumoniae* was detected in swab taken from the left ear. Due to the appearance of convulsions, phenobarbital and midazolam were introduced into therapy. Electroencephalography showed signs of severe encephalopathy. Cerebral MRI with angiography showed meningitis and disseminated multiple inflammatory and ischemic changes in brain tissue. Cranial venous sinuses had a normal caliber and blood flow, with no signs of thrombosis (Figure 2).

On the fifth hospital day, mastoidectomy was done with myringotomy and implantation of ventilation tube. During surgery, we found that tympanic membrane had healed where it spontaneously perforated and after myringotomy, abundant purulent content was obtained from the middle ear. Mastoid cavity was completely filled with inflamed mucosa and granulation tissue. Osteolytic changes were present in the intercellular septa, but bone integrity to the middle and posterior cranial fossa was preserved. Histopathologic findings pointed to a non-specific granulation tissue. Postoperatively, the patient showed an improvement concerning his consciousness and motor skills, but after a few days, we registered an increase in laboratory parameters of inflammation and fever. The antibiotic therapy was changed to cefepime and clindamycin, but without significant improvement in the clinical picture. Medical advisory board had decided that radical tympanomastoidectomy

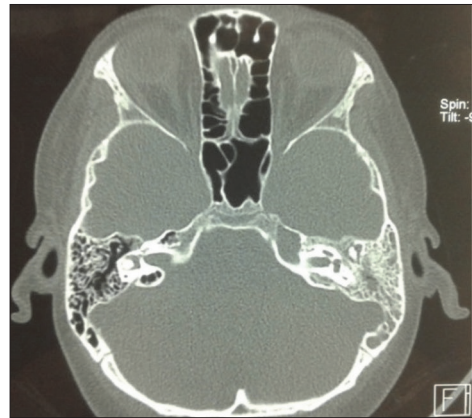


Figure 1. Axial computed tomography scan showed soft tissue opacity of the middle ear, mastoid and petrosal apex on the left side

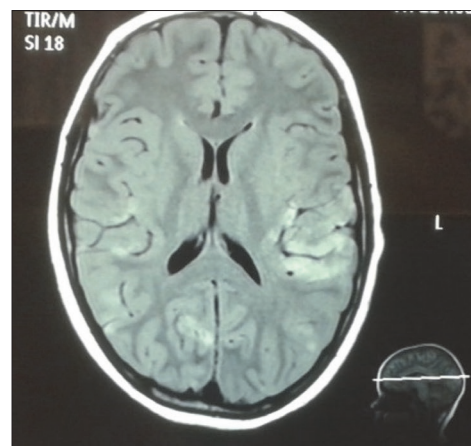


Figure 2. Axial magnetic resonance imaging showed multiple inflammatory and ischemic changes in brain tissue

must be performed in order to provide a more complete removal of the pathological process, and it was done eight days after the first operation.

During hospitalization, the patient received parenteral antibiotic therapy for seven weeks. Because of the long-term antibiotic treatment, toxic hepatitis had developed (AST 620 U/L, ALT 575 U/L). *Mycoplasma pneumoniae* infection, as one of the complications was serologically proven during hospitalization, when azithromycin was included in the treatment. The infection was complicated by hemolytic anemia and the patient received two doses of concentrated red blood cells.

The patient spent 71 days in hospital. He was discharged from the hospital in a good general condition, without the focal motor failure. By applying intensive physical therapy the patient was able to walk independently, sphincter control was normal, he understood orders, but aphasia was present. Due to the inability of oral feeding, the patient was discharged with nasogastric tube that was well tolerated. Finally, the immunological tests performed during hospitalization showed that the patient was immunocompetent.

After he left the hospital, our patient began intensive therapy with a psychologist and a speech therapist. The results were good and this boy has successfully completed

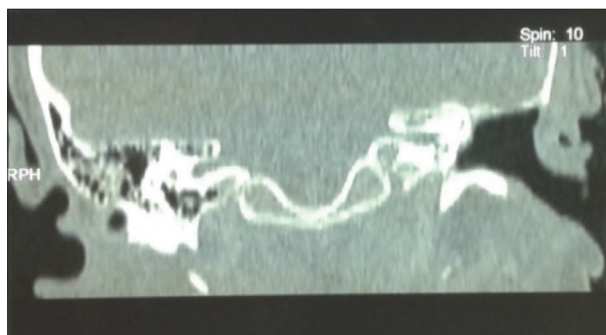


Figure 3. Coronal Computed Tomography scan after radical tympanomastoidectomy showed normal findings

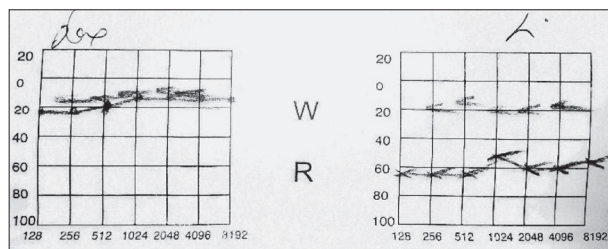


Figure 4. Pure tone audiogram after treatment showed moderate conductive hearing loss in the left ear

fifth grade. On the last medical checkup that was done a year and a half after hospital treatment: clinical and CT findings (Figure 3) were normal and audiometric finding corresponded to surgery performed (Figure 4).

DISCUSSION

The diagnosis of AOM is not always easy, especially when considering the fact that this disease is most common in the first two years of life, and that clinical picture can be dominated by the respiratory and gastrointestinal tract symptoms. For children over six months with the presence of very prominent symptoms and signs of AOM (intense pain that lasts more than 48 hours and body temperature $\geq 39^{\circ}\text{C}$), as well as for children of 6–23 months with bilateral AOM and moderate symptoms and signs of disease, the antibiotic therapy is recommended. In addition, the choice of antibiotics, adequate dose and the length of therapy are very important [1, 2]. Unfortunately, we are still unable to predict which patient will have a poor response or develop severe complications.

Streptococcus pneumoniae is the most common cause of complications of AOM in children and some studies present disturbing data on increasing resistance to antibiotics [4, 8, 9]. Recent studies confirm the hypothesis that serotypes with high invasive potential causes invasive pneumococcal disease in younger patients with less comorbidity [10]. In our case, *Streptococcus pneumoniae* was isolated from the secretions of the left ear, but serotyping had not been done for technical reasons. Clinicians should recommend pneumococcal conjugate vaccine and annual influenza vaccine to all children according to updated schedules [1].

According to literature data, other causes of complications in AOM are *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Haemophilus influenzae*, and *Staphylococcus aureus* [3, 4]. Some studies indicate a possible role of anaerobic bacteria in the occurrence of ICC in pediatric population with acute mastoiditis [8].

The development of otogenic ICC is thought to occur by one of three pathophysiological mechanisms: direct extension of infection through bone weakened by osteomyelitis or cholesteatoma; retrograde spread of infection by thrombophlebitis; or extension of infection along preformed pathways, such as the oval and round windows, or through dehiscence that is the result of congenital malformations. Histological research on temporal bones of the infants who died due to otogenic meningitis, have shown the presence of chronic inflammatory cells in the round window membrane, perilymph, modiolus and cochlear aqueduct, which indicates a possible “silent” route of the infection spread from the middle ear towards the endocranium [11]. Later research on temporal bones indicates the connection between the presence of bacteria in fibrous matrix in the ear with chronic pathologic changes and tympanogenic meningitis in infants. In 82% of the cases, the presence of bacteria was detected in fibrous matrix at different locations in the middle and inner ear, and most often around oval and round window [12]. Chronic inflammatory changes in the middle ear behind the intact eardrum and the absence of otologic symptoms can lead to occurrence of serious complications in infants [11, 12]. In our case, the fulminant course of the disease indicates a possible hematogenic spread of the infection from the middle ear to the endocranium, with the occurrence of a severe form of meningoenzephalitis. All data point to an accidental infection in an immunocompetent child.

Chronic otitis media with cholesteatoma is the most common cause of ICC [13, 14]. Đerić et al. [13] recorded 114 cases of otogenic ICC in an extensive retrospective study over the period of 23 years. The most common was meningitis, followed by brain abscess and lateral sinus thrombosis. Half of the patients had two or more complications at the same time, and otogenic abscess were often combined with meningitis. For that reason, the authors emphasize the importance of CT scan in the diagnostics of the ICC, especially in the abscesses of a “silent” clinical course, when the treatment of the active phase of chronic otitis with antibiotics can conceal early symptoms of the occurrence of this complication [15]. Dankuc et al. [16] describe a simultaneous existence of ECC and ICC in an adult patient with the exacerbation of chronic suppurative otitis. The authors described the protective role of the dura mater in the localization of subdural abscess, but also a possibility of further spread of the infection by hematogenic way into the brain tissue with the creation of the encephalitis focus and brain abscess later.

In the era of antibiotics, ICC of AOM is rarely seen. De Oliveira Penido et al. [3] recorded only ten cases of AOM with ICC during the period of 22 years, and observed that the complications generally occur in people younger than 15, as well as in the elderly population. Mattos et al. [4]

recorded 26 cases of ICC in children with AOM during the 15-year period. Interestingly, meningitis was recorded in one case only, while encephalitis was not recorded in any case. Leskinen and Jero [17] in a 10-year retrospective study at pediatric population described extradural abscess with meningitis as the only ICC of AOM. Zernotti et al. [18] describe one case of encephalitis and subdural empyema as a complication of AOM. In contrast, Krivopalov et al. [19] recorded meningoencephalitis as a complication of AOM in 15.4% of adult patients.

During the treatment of our patient, we were faced with several dilemmas. How long does one need to wait for surgical treatment, due to the fact that the patient is comatose? Which surgical method is the right choice in such a case? Zanetti et al. [20] in a study of 45 children with acute mastoiditis discovered ICC in 28.9% of cases. They advised mastoidectomy in the first 48–72 hours, if neurological status allows this. In two cases with severe ICC was performed a surgery of the canal wall down. Other authors also propose extended mastoidectomy in the treatment of meningoencephalitis, which is the result of AOM [19]. In a study published by De Oliveira Penido et al. [3] all patients with AOM and ICC were surgically treated. Neurosurgical treatment was performed in six patients in order to evacuate the cerebral abscess, while four patients were treated with otosurgical procedures (tympanocentesis in three patients and tympanomastoidectomy in one patient). In our case, convulsive seizures and neurological status did not allow the surgery in the first few days, and mastoidectomy with the implantation of ventilation tube did not lead to an improvement of consciousness and general condition of the patient.

Consequently, it raises the following question whether it was necessary to perform radical surgery immediately in order to have a more complete removal of the pathological process, considering the cause of infection and inflammation, which is affecting deep retrofacial and infracochlear cell tract together with retrolabyrinthine cells and petrous apex.

During the treatment of our patient, we met a number of complications, such as the inability of oral feeding, inability to control sphincter, confinement to bed, toxic hepatitis, infection by *Mycoplasma pneumoniae*, and hemolytic anemia. Considering all the above, it is not surprising that our patient stayed in the hospital for 71 days, which is significantly higher compared to some data from the literature [3]. Some authors recorded that 29.4% of patients with otogenic ICC has neurological sequelae in the form of abducens nerve palsy, reduction of intellectual capacity, dysmetria, and dysarthria [3]. In our patient neurological sequelae in the form of occasional agitation and aphasia significantly improved by adequate medical teamwork, while unilateral conductive hearing loss is only auditory sequelae.

To conclude, meningoencephalitis is an unusual and rare complication of AOM. Fulminant course of the disease requires urgent diagnostic procedure and multidisciplinary approach to the treatment. Surgical treatment of the ear, which caused the complication, should not be delayed, and the choice of surgical method must be adapted to each patient individually. Hospital treatment of these patients is often prolonged and auditory and neurological sequelae are substantial and require long-term treatment.

Conflict of interest: None declared.

REFERENCES

- Lieberthal AS, Carroll AE, Chonmaitree T, Ganiats TG, Hoberman A, Jackson MA, et al. The diagnosis and management of acute otitis media. *Pediatrics*. 2013; 131(3):964–99.
- Le Saux N, Robinson JL, Canadian Paediatric Society Infectious Diseases and Immunization Committee. Management of acute otitis media in children six months of age and older. *Paediatr Child Health*. 2016; 21(1):39–44.
- De Oliveira Penido N, Chandrasekhar SS, Borin A, De Albuquerque Maranhao AS, Gurgel Testa JR. Complications of otitis media – a potentially lethal problem still present. *Braz J Otorhinolaryngol*. 2016; 82(3):253–62.
- Mattos JL, Colman KL, Casselbrant ML, Chi DH. Intratemporal and intracranial complications of acute otitis media in a pediatric population. *Int J Pediatr Otorhinolaryngol*. 2014; 78(12):2161–4.
- Yorgancilar E, Yildirim M, Gun R, Bakir S, Tekin R, Gocmez C, et al. Complications of chronic suppurative otitis media: a retrospective review. *Eur Arch Otorhinolaryngol*. 2013; 270(1):69–76.
- Osma U, Cureoglu S, Hosoglu S. The complications of chronic otitis media: report of 93 cases. *J Laryngol Otol*. 2000; 114(2):97–100.
- Dowell SF, Butler JC, Giebink GS, Jacobs MR, Jernigan D, Musher DM, et al. Acute otitis media: management and surveillance in an era of pneumococcal resistance – a reports from the drug-resistant *Streptococcus pneumoniae* Therapeutic Working Group. *Pediatr Infect Dis J*. 1999; 18(1):1–9.
- Zevallos JP, Vrabec JT, Williamson RA, Giannoni C, Larrier D, Sulek M, et al. Advanced pediatric mastoiditis with and without intracranial complications. *Laryngoscope*. 2009; 119(8):1610–5.
- Anthonsen K, Høstmark K, Hansen S, Andreassen K, Juhlén J, Homøe P, et al. Acute mastoiditis in children: a 10-year retrospective and validated multicenter study. *Pediatr Infect Dis J*. 2013; 32(5):436–40.
- Ahl J, Littorin N, Forsgren A, Odenholt I, Resman F, Riesbeck K. High incidence of septic shock caused by *Streptococcus pneumoniae* serotype 3 – a retrospective epidemiological study. *BMC Infect Dis*. 2013; 13:492–9.
- Djerić D, Schachern P, Paparella M, Jaramillo M, Haruna S, Bassioni M. Otitis media (silent): a potential cause of childhood meningitis. *Laryngoscope*. 1994; 104(12):1453–60.
- Yildirim-Baylan M, Schachern P, Tsuprun V, Shiabata D, Paparella M, Cureoglu S. The pathology of silent otitis media: A predecessor to tympanogenic meningitis in infants. *Int J Pediatr Otorhinolaryngol*. 2014; 78(3):451–4.
- Đerić D, Arsović N, Đorđević V. Pathogenesis and methods of treatment of otogenic brain abscess. *Med Pregl*. 1998; 51(1-2):51–5.
- Nešić V, Janošević Lj, Stojičić G, Janošević S, Rasulić L, Babac S, et al. Otogenic brain abscess. *Srp Arh Celok Lek*. 2002; 130:389–93.
- Đerić D, Đorđević V, Đurović B. A quiet clinical course in an otogenic brain abscess. *Med Pregl*. 1999; 52(11-12):505–7.
- Dankuc D, Milošević D, Savić L. Simultaneous extracranial and intracranial otogenic complications. *Med Pregl*. 2000; 53(7-8):409–12.
- Leskinen K, Jero J. Complications of acute otitis media in children in southern Finland. *Int J Pediatr Otorhinolaryngol*. 2004; 68(3):317–24.
- Zernotti ME, Casarotto C, Tosello ML, Zernotti M. Incidence of complications of otitis media. *Acta Otorrinolaringol Esp*. 2005; 56(2):59–62.
- Krivopalov AA, Yanov YK, Astashchenko SV, Shcherbuk AY, Artyushkin SA, Vakhrushev SG, et al. Features of otogenic intracranial complications at the present stage. *Vestn Khir Im II Grek*. 2015; 174(6):68–79.
- Zanetti D, Nassif N. Indications for surgery in acute mastoiditis and their complications in children. *Int J Pediatr Otorhinolaryngol*. 2006; 70(7):1175–82.

Менингоенцефалитис као компликација акутног запаљења средњег ува код 11-годишњег детета

Зоран Дудварски^{1,2}, Ненад Арсовић^{1,2}, Снежана Јешић^{1,2}, Владимир Нешић^{1,2}, Биљана Међо^{1,3}, Димитрије Николић^{1,4}

¹Универзитет у Београду, Медицински факултет, Београд, Србија;

²Клинички центар Србије, Клиника за оториноларингологију и максилнофацијалну хирургију, Београд, Србија;

³Универзитетска дечја болница, Јединица интензивне неге, Београд, Србија;

⁴Универзитетска дечја болница, Одељење неурологије, Београд, Србија

САЖЕТАК

Увод Акутно запаљење средњег ува је веома често обољење у раном дечјем узрасту. Отogene компликације се деле на екстракранијалне и интракранијалне. Увођење антибиотика је значајно смањило учесталост интракранијалних компликација, али оне још увек постоје. Клиничка слика се обично брзо развија уз преминацију неуролошких симптома.

Приказ болесника Дечак стар 11 година је примљен у терцијерну здравствену установу због повишене телесне температуре, узнемирености, измењеног понашања и поремећаја стања свести. На основу анамнезе, клиничког прегледа, компјутеризоване томографије, магнетне резонанце и лумбалне пункције утврђено је да се ради о менингоенцефалитису као компликацији акутног запаљења средњег ува. Осим интензивне антибиотске и симптоматске терапије, спроведено је и хируршко лечење: најпре мастоидектомија са имплан-

тацијом вентилационе цевчице, а потом радикална тимпаномастоидектомија, јер није дошло до очекиваног побољшања. Лечење је било праћено бројним компликацијама, као што су токсични хепатитис, инфекција са *Mycoplasma pneumoniae* и хемолитичка анемија. Лечење је трајало 71 дан, а болесник је отпуштен из болнице у добром општем стању, без фокалних моторних испада.

Закључак Менингоенцефалитис је неуобичајена и ретка компликација акутног запаљења средњег ува, која захтева хитну дијагностику и мултидисциплинарни приступ у лечењу. Хируршко лечење ува не треба одлагати, а избор хируршке методе мора бити прилагођен. Болничко лечење је често продужено, а аудиторне и неуролошке секвеле су значајне и захтевају дуготрајан третман.

Кључне речи: акутно запаљење средњег ува; интракранијалне компликације; деца